

Mating Scheme For Production Of HbA Replacement Mice

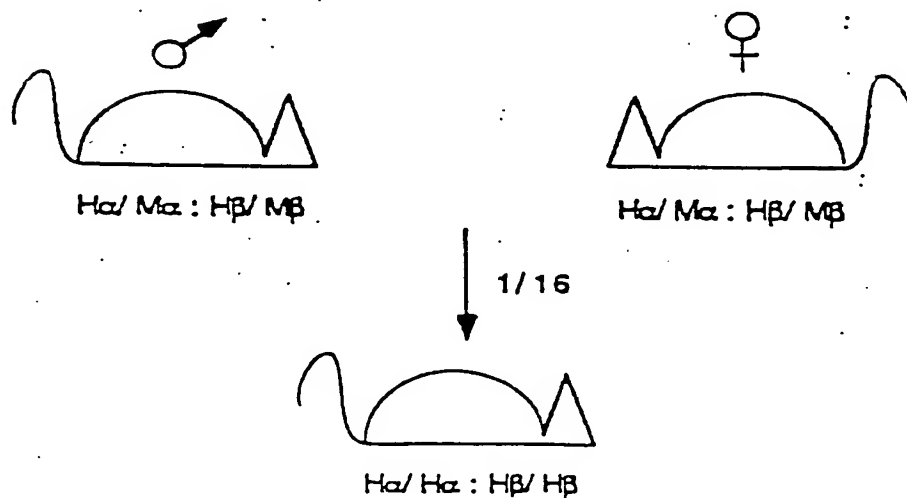
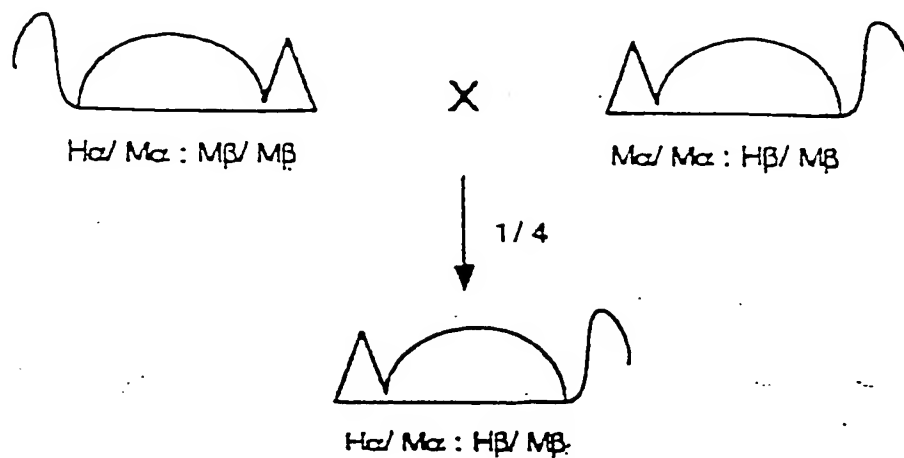
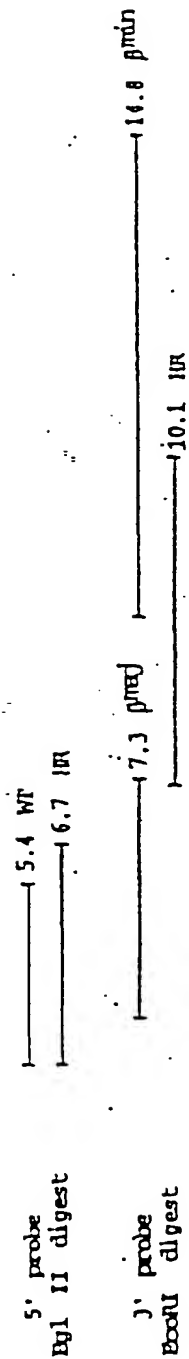
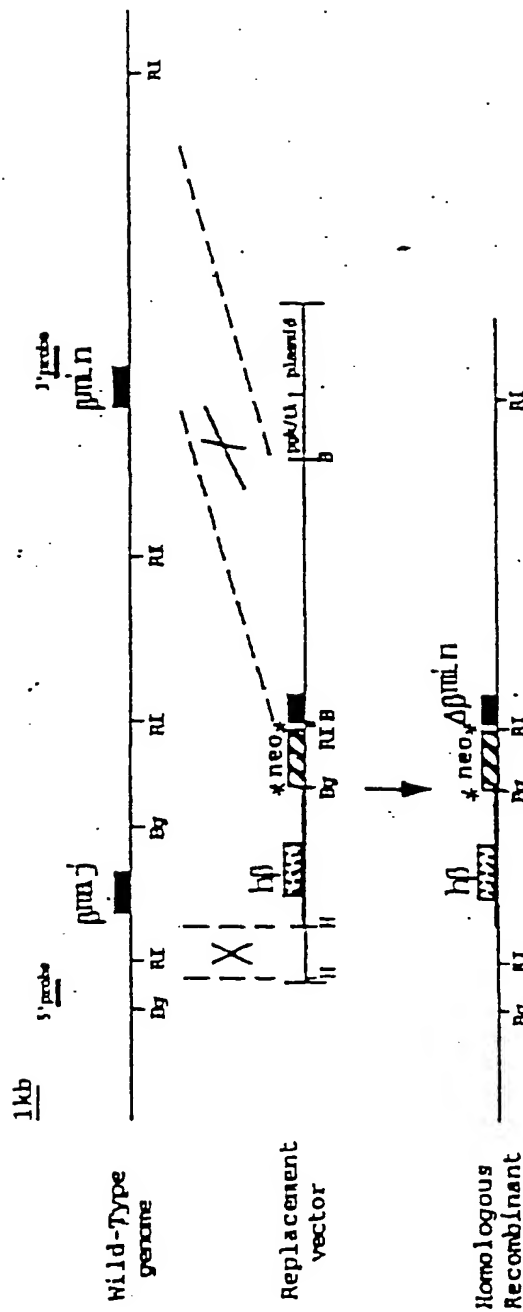
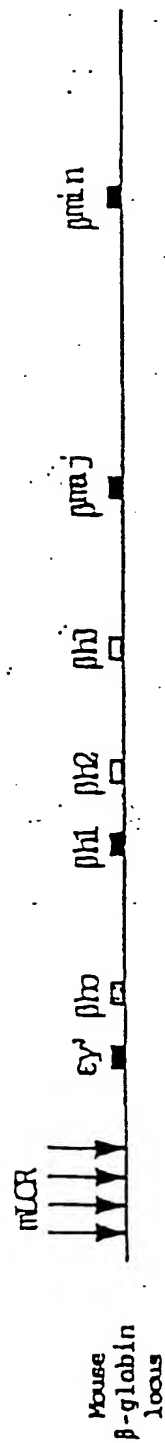


FIG. 1

FIG. 2

Mouse β KO/human β replacement



Human Replacement Of The Mouse β -Globin Locus

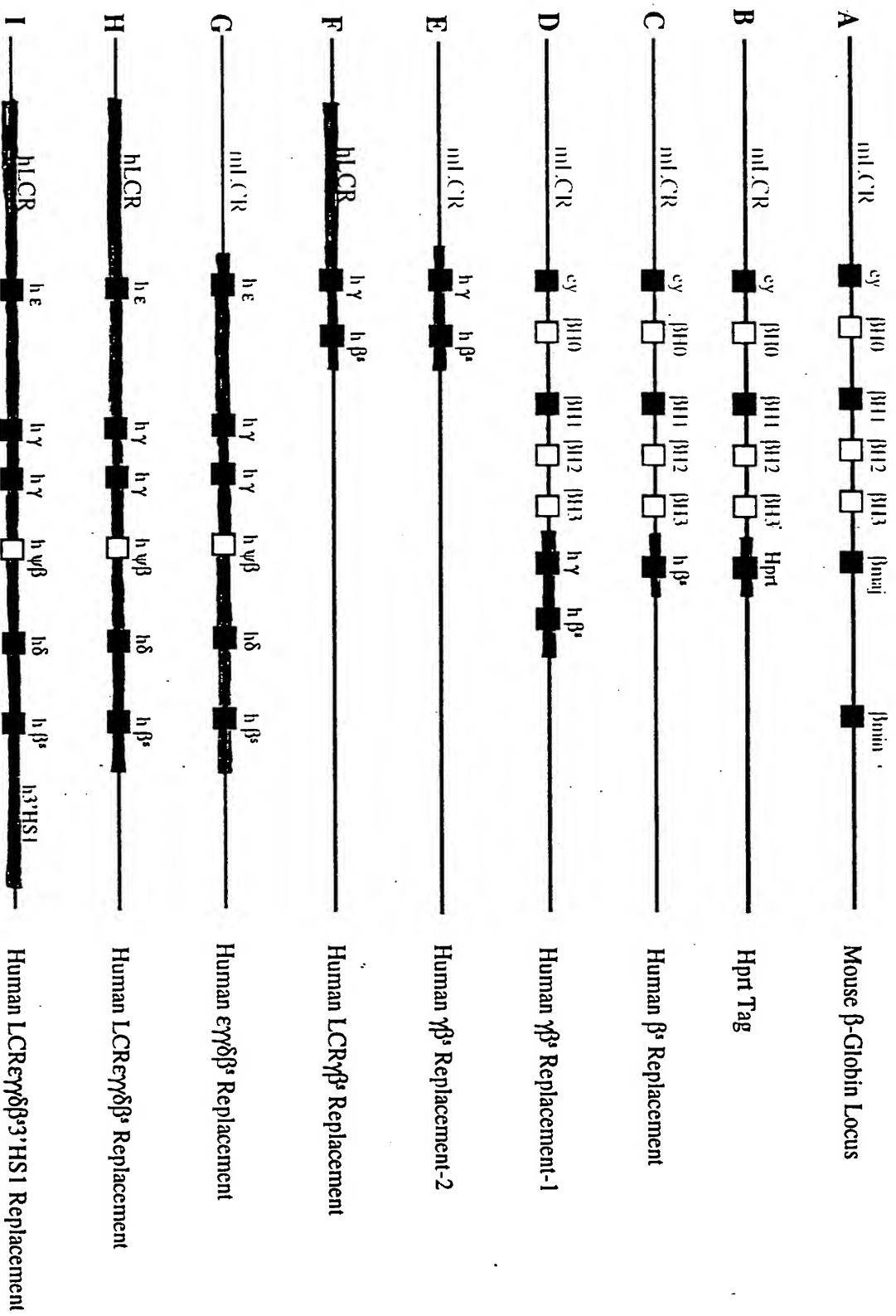


Fig. 3

Human Replacement Of The Mouse α -Globin Locus

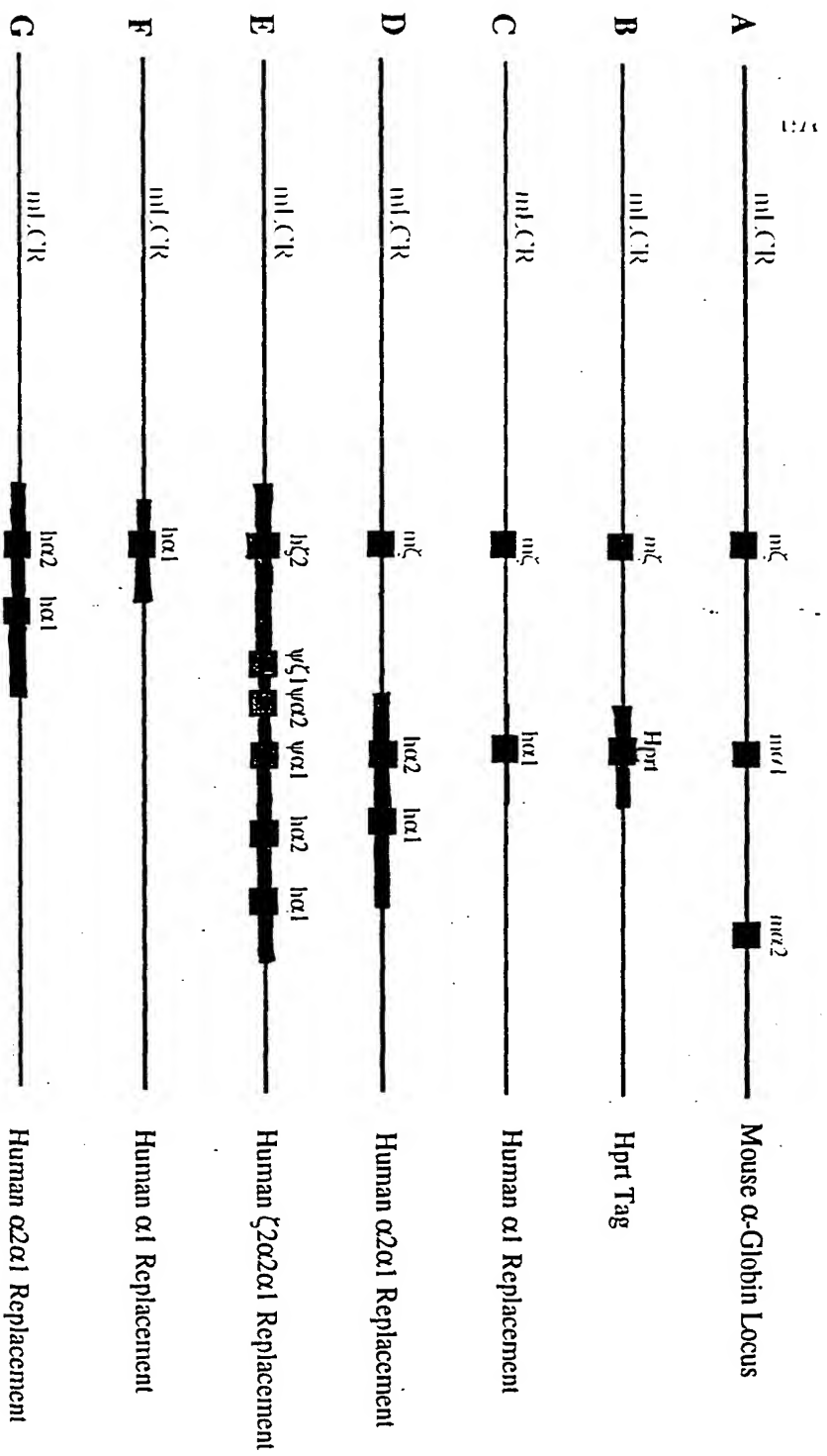


Fig. 4

Production Of Transgenic HbF \rightarrow HbA Mice
 (Doubly Homozygous For Mouse α -Globin And β -Globin Deletions)

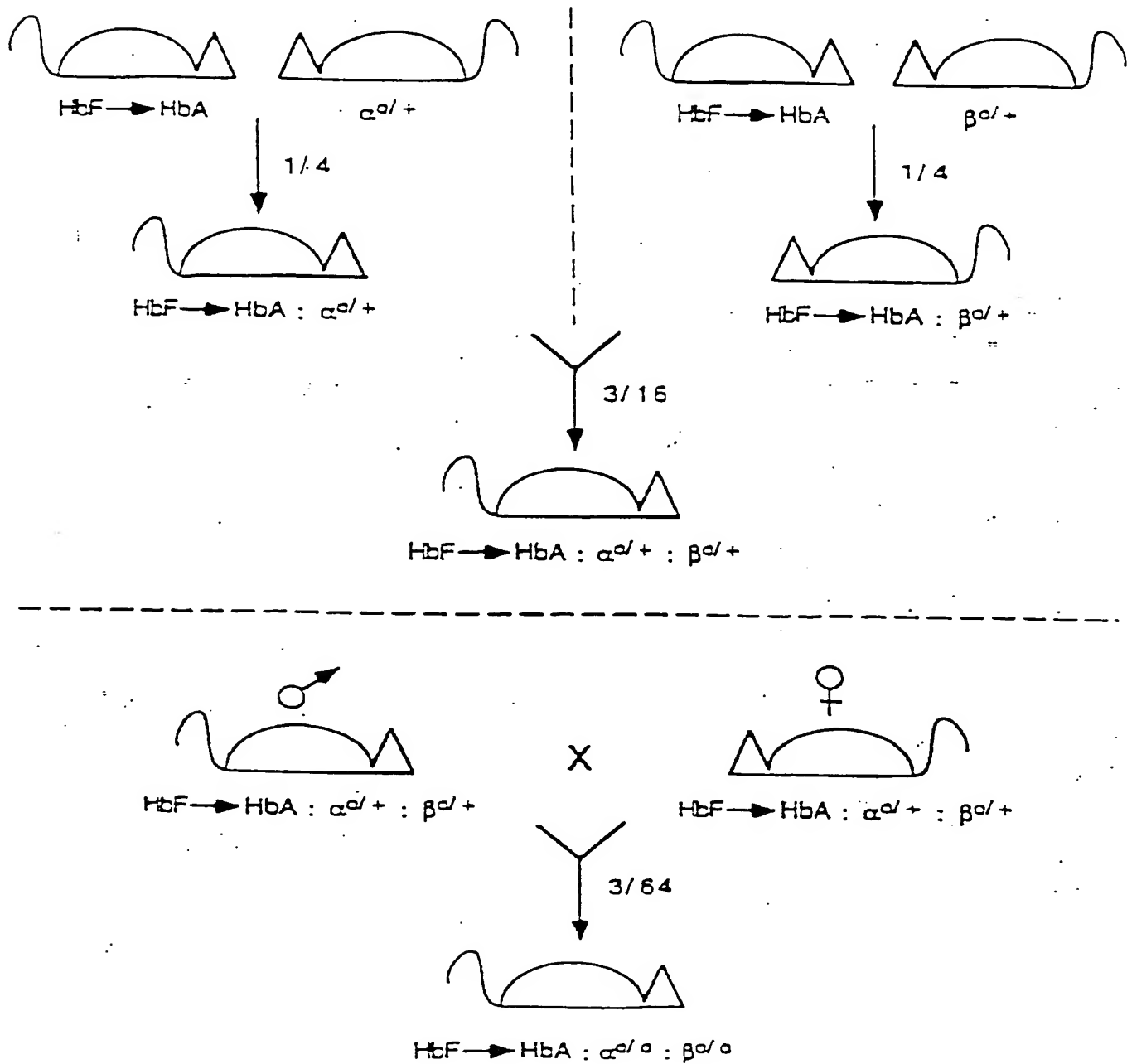
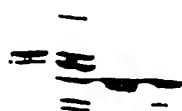


FIG. 5

Isoelectric Focusing Gel Of Transgenic Mouse Hemolysates

1 2 3 4

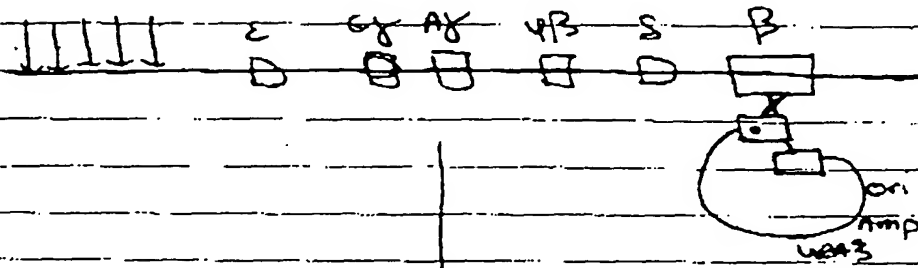


1. Mouse Control
2. HbF \rightarrow HbA : $\alpha^{+/+} : \beta^{+/+}$ Mouse
3. HbF \rightarrow HbA : $\alpha^{0/0} : \beta^{0/0}$ Mouse
4. Human AA Control

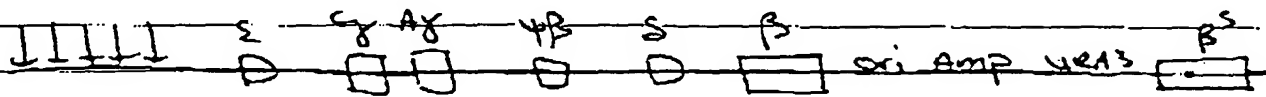
FIG. 6

FIG. 7

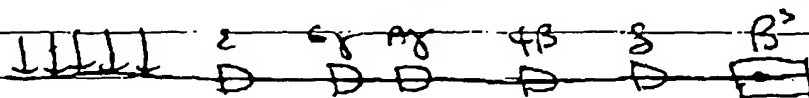
YAC

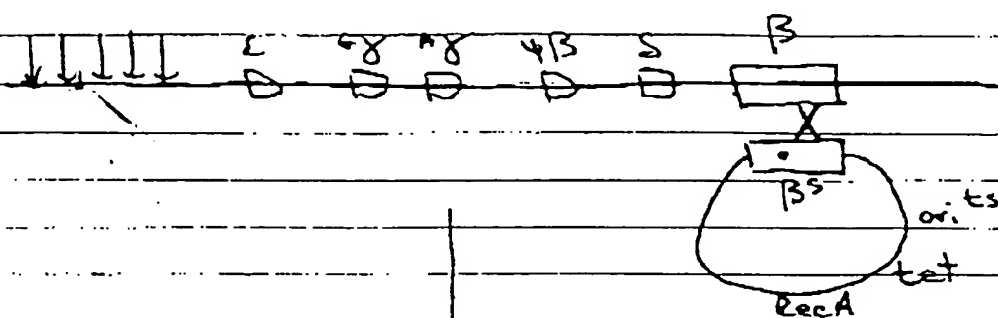


select for URA3⁺

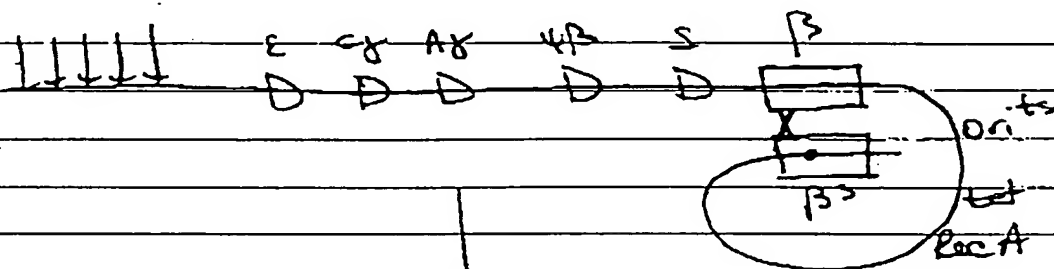
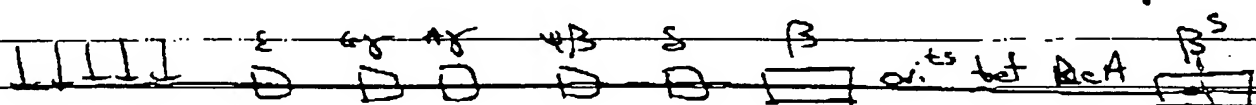


select for URA3
(5-Fluoro-uracil)



BAC

select for tet^R at $43^\circ C$
(non-permissive temp for ori^{ts})



select for tet^S (Fusaric Acid)
at $37^\circ C$

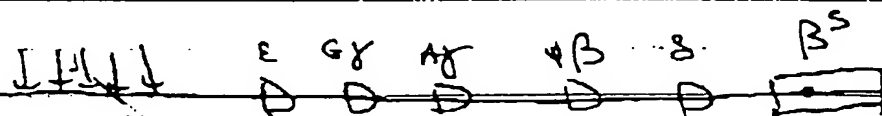


FIG. 9A

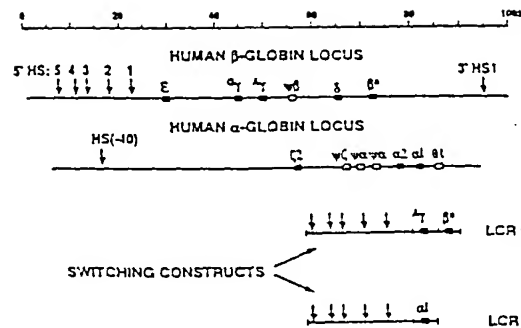


FIG. 9B

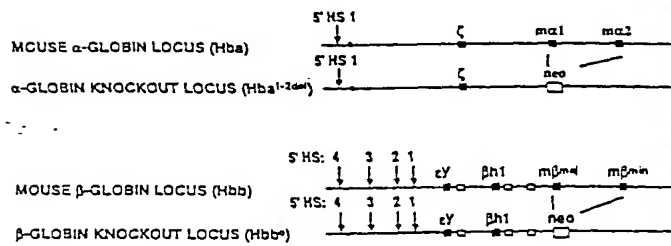
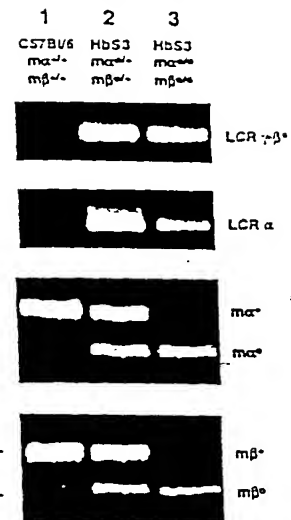


FIG. 9C



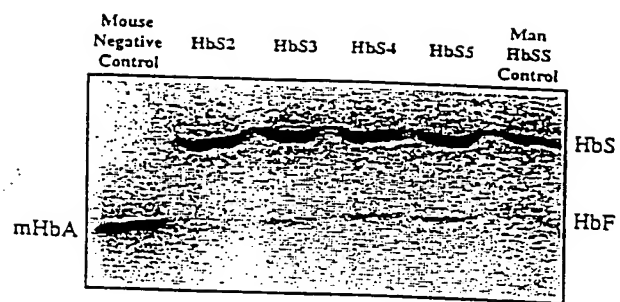


FIG. 10

FIG. 11A

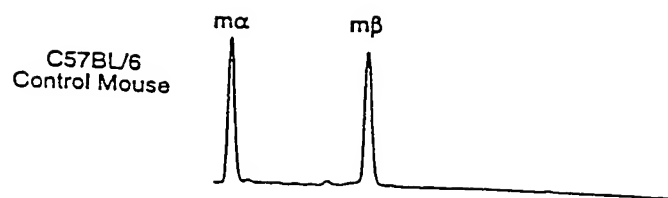


FIG. 11B



FIG. 11C

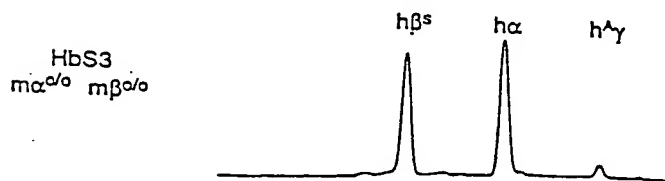
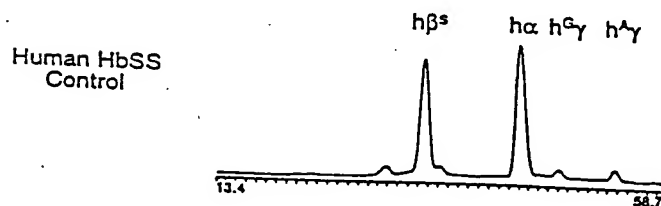


FIG. 11D



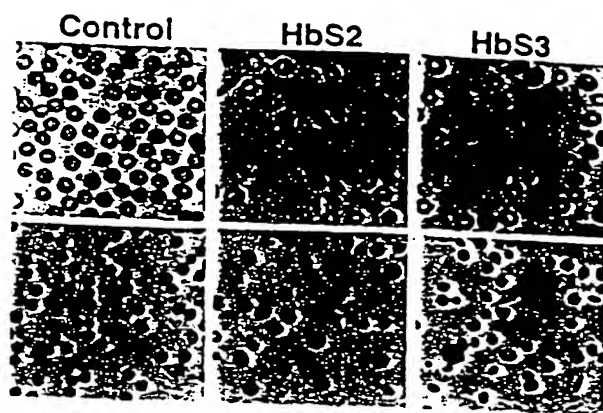


FIG. 12

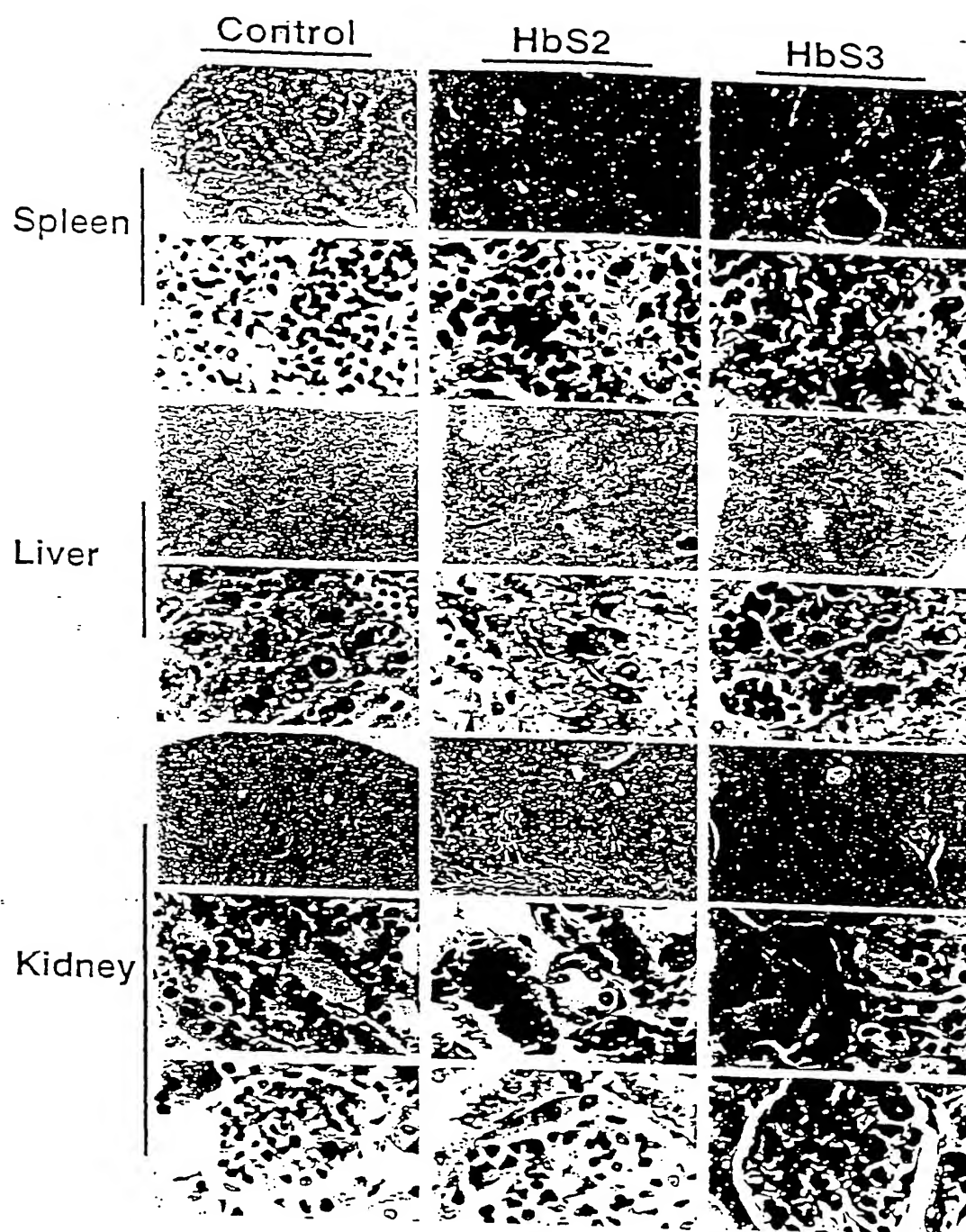


FIG. 13

FIG. 14A

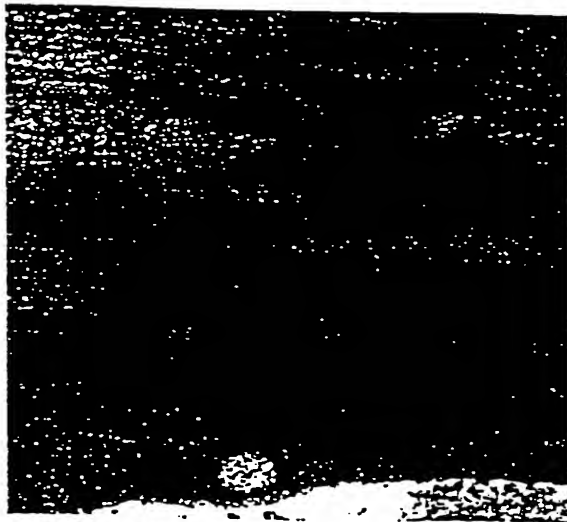


FIG. 14B



Hemoglobin Switching In HbA Mice

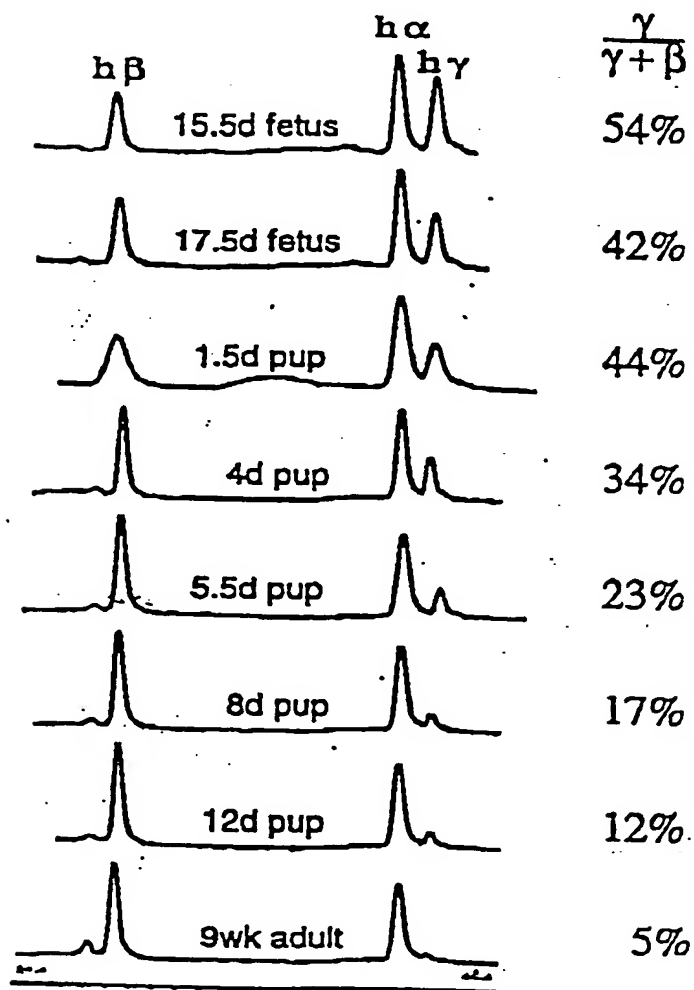


FIG. 15

**Increasing HbF Levels In HbS Mice:
Crossing The HbS 3 and HbF Lines**

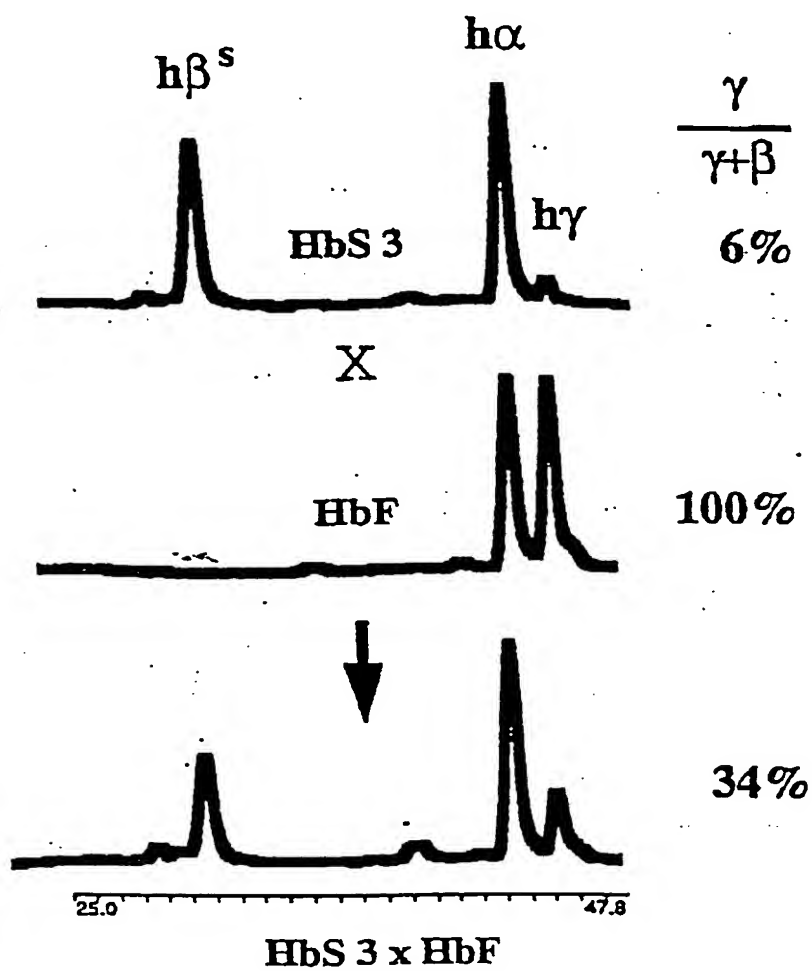


FIG. 16